



Uehiro Laboratory for my iPS Cell Research

iPS Cell Stock

On October 2, Kyoto University Hospital announced the start of an investigator-initiated clinical trial for type 1 diabetes patients from January 2025. In addition, on November 8 (Japan time), the results of a clinical study conducted by Professor Koji Nishida and his colleagues at Osaka University on corneal epithelial stem cell exhaustion, demonstrating safety and efficacy, were published in the international medical journal *The Lancet*. CiRA Foundation's iPS cell stock is used as raw material for transplantation cells in these clinical trials and studies. To provide iPS cells of better quality, we continue to work closely with organizations using our iPS cell stock and utilize new knowledge gained through the progress of research in the production and quality evaluation of iPS cells.



“my iPS Project” Research Facility Completed in Nakanoshima

The “my iPS Project,” which produces high-quality and reasonably priced iPS cells from one's own somatic cells, has opened a research facility and an adjacent facility, the Uehiro Laboratory for my iPS Cell Research, on the 7th floor of the Nakanoshima Cross building in Nakanoshima, Kita-ku, Osaka City. It includes an open laboratory for conducting experiments and approximately 620 m² of office space. Researchers from the CiRA Foundation and collaborating universities and companies will conduct research and development to promote the spread of iPS cell technology, including automated production of iPS cells, at the new facility.



The sign for the
Uehiro Laboratory
for my iPS Cell Research
at the entrance



Start of Physician-initiated Clinical Trial on Transplantation of iPS-derived Islet Cell Sheets

On October 2, Kyoto University Hospital announced the start of an investigator-initiated clinical trial for type 1 diabetes patients in January 2025 to demonstrate the safety and efficacy of iPS cell-derived islet cell sheets in patients eligible for islet transplantation.

The iPS cell-derived islet cell sheets to be used for transplantations are made from the CiRA Foundation's iPS cell stock and were developed by a research group led by CiRA Junior Associate Professor Taro Toyoda as part of the T-CiRA program, a joint research project between the Center for iPS Cell Research and Application (CiRA) at Kyoto University and Takeda Pharmaceutical Company Limited.



Assoc. Prof. Toyoda explains his research ©CiRA

Explaining the results of his research during a press briefing, Assoc. Prof. Toyoda said, "I have been working on the in vitro generation of islet cells from human iPS and ES cells since around 2010. Although there is a big gap between basic research and clinical application, through the T-CiRA program and joint research with several companies, we have been able to construct a practical system, including a culture medium exchange system and the development of large sterile culture bags, to produce the hundreds of millions of cells required for transplantation. Among the many challenges, one of the most difficult was ensuring safety. It is challenging to guarantee that not even a few non-target cells are among several hundred million cells. After overcoming these challenges, we are now ready to proceed to clinical trials. I believe our long-term, stable research infrastructure has greatly assisted us in reaching this point. I will continue dedicating my research efforts to ensure the success of this clinical trial."

The technology developed by Assoc. Prof. Toyoda and his colleagues has now been taken over by Orizuru Therapeutics, and the iPS cell-derived islet cell sheets will be transplanted into patients in this clinical trial by physicians at Kyoto University Hospital as the company's investigational product.

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For details about this clinical trial, please refer to the official website of the Kyoto University Hospital.
<https://www.kuhp.kyoto-u.ac.jp/press/20241002.html>

Clinical Research on Corneal Opacity Due to Limbal Stem Cell Deficiency

The results of clinical research on corneal opacity due to limbal stem cell deficiency by a research group led by Professor Koji Nishida of Osaka University, who is also a board member of the CiRA Foundation, were published in the international medical journal *The Lancet* on November 8 (Japan time).

As a co-investigator of this clinical study, the CiRA Foundation was in charge of providing the iPS cell stock used as raw material for the transplanted allogeneic corneal epithelial cell sheets for four patients, and genome analysis.

Reductions in corneal opacity and improvements in corrected visual acuity and the stage of corneal epithelial stem cell exhaustion were observed in all patients, with no reports of safety issues such as tumor formation or rejection. The results demonstrating safety and efficacy were summarized in the paper.

Prof. Nishida and his research group aim to develop this technology into a standard medical treatment through clinical trials in the future.



Genome Analysis Unit Head
Masaki Nomura

INTERVIEW MASAKI NOMURA

We interviewed Masaki Nomura, co-author of the paper on this clinical study and head of the Genome Analysis Unit at the CiRA Foundation.

Q1

What is the purpose of genome analysis in clinical research using iPS cells?

In clinical research, the safety of cells used for transplantation is confirmed through tumorigenicity tests. Although it is difficult to accurately evaluate safety based solely on the results of genome analysis, it is conducted to make a comprehensive judgment in combination with the results of other tests. Genome analysis is also required by the guidelines for regenerative medicine.

Q2

What exactly do you do?

We use next-generation sequencers to obtain the entire DNA sequence (whole genome) of cells used as raw materials for establishing iPS cells and cells used for transplantation. We compare these sequences to determine whether the DNA sequence has changed in cells to be transplanted. The work is performed by the Genome Analysis Unit.

Q3

Thoughts on Practical Application

This year's Nobel Prize in Physics was awarded to Dr. John Hopfield, a pioneer in artificial intelligence. Although there have been periods of stagnation in the field, research on artificial intelligence has continued for over 50 years, with many amazing breakthroughs and practical applications. The iPS cell technology has progressed even more rapidly and is now on the brink of real-world applications. It gives me great pleasure to be able to witness the dawn of this technology. Although there remain many challenges ahead for their medical applications, I want to make every effort to deliver high-quality medical treatments using iPS cell technology to patients as soon as possible.

Designated as a research institute eligible for Grants-in-Aid for Scientific Research funding by MEXT

On August 7, 2024, the research and development center of the CiRA Foundation was designated by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) as a research institute, as stipulated in Article 2 of the Regulations for Handling Grants-in-Aid for Scientific Research. We will continue to focus on the “my iPS project” while utilizing public research funds to develop a closed-type automated culture system through joint research with companies to reduce the production costs of iPS cells.



Designated as an eligible recipient of personal residential tax-deductible donations by Osaka Prefecture and Osaka City

CiRA Foundation has been designated by Osaka Prefecture (as of July 29, 2024) and Osaka City (as of September 6, 2024) as an entity eligible for receiving personal residential tax-deductible donations. As a result, in addition to Kyoto Prefecture and Kyoto City residents, individuals residing in Osaka Prefecture and Osaka City can now receive a personal residential tax credit for donations (donations and membership fees) made to the CiRA Foundation on or after January 1, 2024, by filing a tax return.



Kyoto City accepts “Hometown Tax Payments” throughout the year from corporations

To promote the practical use of iPS cells and to support research and development in the field of life science conducted by small and medium-sized enterprises and university researchers in Kyoto City, the city has expanded the donation period for “Corporation-oriented Hometown Tax Payments,” previously offered only for a limited time, to the entire year starting this fiscal year.

